IMPROVING POLYPEPTIDE PRODUCTION IN ANIMAL CELL CULTURE

Abstract of the Disclosure

A method of producing a polypeptide in fed batch cell culture is provided which involves an initial cell growth phase and a distinct production phase. In the initial growth stage, animal cells having nucleic acid encoding the polypeptide are cultured at a starting osmolality of about 280-330 mOsm in the presence of a concentration of glucose controlled throughout the culturing to be within a range between about 0.01 and 1g/L. This is followed by a production phase, where the cultured animal cells of the growth phase are inoculated at a cell seed density of at least 1.0×10^6 cells/mL and the cells are cultured at a starting osmolarity of about 400-600 mOsm in the presence of a concentration of glucose controlled throughout the culturing to be within a range between about 0.01 and 1g/L. Preferably, the glutamine concentration in the cell culture medium is simultaneously controlled in order to curtail production of lactic acid and ammonia which result from unnecessarily high glutamine concentrations. During the growth phase, production of potentially detrimental metabolic waste products, such as lactic acid, is controlled thereby curtailing the increase of osmolality due to accumulation and neutralization of waste products. Thus, the cell growth can be improved. In the production phase, the cell culture conditions are modified in order to arrest or reduce cell growth and thereby direct nutrient utilization toward production, as opposed to cell growth. Overall, it is intended that the method results in an improvement in specific productivity, reduction in production run times and/or an increase in final product concentration.